TENT COOPERATION TREATY

REC'D 05 MAY 2004

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

			
Applicant's or agent's file reference	FOR FURTHER ACTION See Form PCT/IPEA/416		
HeL/AO 49908			
International application No.	International filing date (day/month/year	Priority date (day/month/year)	
PCT/SE 2003/000092	21.01.2003	21.01.2002	
International Patent Classification (IPC) or	r national classification and IPC		
A61K 9/20			
Applicant			
Galenica AB Medeon et	-1		
Garenica Ab Medeon et	ar		
	liminary examination report, established insmitted to the applicant according to Ar	by this International Preliminary Examining ticle 36.	
2. This REPORT consists of a total o	of 7 sheets, including this	cover sheet.	
3. This report is also accompanied by	ANNEXES, comprising:		
N			
	and to the International Bureau) a total o		
and/or sheets	lescription, claims and/or drawings which containing rectifications authorized by the e Instructions).	have been amended and are the basis of this report is Authority (see Rule 70.16 and Section 607 of the	
		Ithority considers contain an amendment that goes	
beyond the dis	sclosure in the international application a	s filed, as indicated in item 4 of Box No. I and the	
Supplemental	Box.		
b (sent to the Internation	nal Bureau only) a total of (indicate type	and number of electronic carrier(s))	
, containing a sequence listing and/or tables related thereto, in computer			
readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).			
4. This report contains indications rel	lating to the following items:		
Box No. I Basis of	the report		
Box No. II Priority			
Box No. III Non-esta	ablishment of opinion with regard to nove	elty, inventive step and industrial applicability	
	unity of invention	,	
	•	rd to novelty, inventive step or industrial	
	ility, citations and explanations supporting	g such statement	
Box No. VI Certain o	documents cited		
Box No. VII Certain o	defects in the international application		
Box No. VIII Certain o	observations on the international applicat	on	
Date of submission of the demand Date of completion of this report		A	
2000 of Submission of the defining	Date of comple	tion of this report	
20.08.2003		204	
	27.04.20		
Name and mailing address of the IPEA/SE Patent- och registreringsverket	Authorized off	cer	
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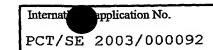
International a tion No.

PCT/SE 2003/000092

Box	No. I	Ba	nsis of the report	
1.	With 1	regard to	o the language, this report is based on the international application in the language icated under this item.	n which it was filed, unless
		This rep	port is based on a translation from the original language into the following language is the language of a translation furnished for the purposes of:	
			international search (under Rules 12.3 and 23.1(b))	
		Ħ	publication of the international application (under Rule 12.4)	
		H	international preliminary examination (under Rules 55.2 and/or 55.3)	
2.	furnisi	hed to th	to the elements of the international application, this report is based on (replacem he receiving Office in response to an invitation under Article 14 are referred to in this mexed to this report):	ent sheets which have been s report as "originally filed"
		the int	ternational application as originally filed/furnished	
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			uence listing and/or any related table(s) - see Supplemental Box Relating to Sequence I	isting.
3.		The a	mendments have resulted in the cancellation of:	
			the description, pages	
		Ħ	the claims, Nos.	
		Ħ	12 1 - 1 - 15 -	
		H		
		H		
		Ш	any table(s) related to the sequence listing (specify):	
4.		This made	report has been established as if (some of) the amendments annexed to this report a c, since they have been considered to go beyond the disclosure as filed, as indicated in c)).	nd listed below had not been the Supplemental Box (Rule
			the description, pages	
			the claims, Nos.	•
		同	the drawings, sheets/figs	
		一	the sequence listing (specify):	
			any table(s) related to the sequence listing (specify):	
	TA			
1	If iten	n 4 appl	lies, some or all of those sheets may be marked "superseded."	

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:
the entire international application
claims Nos. 1-5, partly
because:
the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
·
•
the description, claims or drawings (indicate particular elements below) or said claims Nos. 1-5 are so unclear that no meaningful opinion could be formed (specify):
Present claims 1-5 relate to a composition-forming process which is defined in part by the properties of the substances that are incorporated into the composition, the substances used described in general terms, as well as the properties of the composition thus produced. The expressions that describe those properties (non-swellable, oil, surfactant, polar liquid, self-emulsifying, self-dispersing and immediate/
the claims, or said claims Nos are so inadequately supported
by the description that no meaningful opinion could be formed.
no international search report has been established for said claims Nos.
the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
the written form has not been furnished
does not comply with the standard
the computer readable form has not been furnished
does not comply with the standard
the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-bis of the Administrative Instructions.
See Supplemental Box for further details.



Supplemental Box

In case the space in any of the preceding boxes is not sufficient. Continuation of: Box III.1

release) are not always explicitly used in the literature. Furthermore, support within the meaning of Article 6 PCT is to be found for only a small proportion of the compounds that fall under the properties mentioned above. Thus, a complete search of the whole scope of the claims cannot be performed.

The search has been carried out for a process which involves those compounds that are listed in the description.

Further, the search has covered the general aspects of the invention to some extent, although it lacks the necessary the definition the subject of precision in Consequently, the search for the general concept of a process for the preparation of a self-dispersing or self-emulsifying immediate release tablet will retrieve a pertinent document only if this concept is described in general terms in a reference. Specific processes or tablets previously known and falling under the general concept - but failing to mention this fact - are likely not to be revealed in such a search.

Consequently, the opinion is formed on basis of the search performed.

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		Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
Box No.	. V	Reasoned statement tilder Article 35(2) with regard to
		citations and explanations supporting such statement
		C1000010100

	- · ·
1	Statement

Novelty (N)	Claims Claims	1-5	YES NO
Inventive step (IS)	Claims Claims	1-5	YES NO
Industrial applicability (IA)	Claims Claims	1-5	YES NO

2. Citations and explanations (Rule 70.7)

Documents from the international search report:

- A. Schwarz J. et al., Increased bioavailability of coenzyme Q-10 in self-emulsifying controlled release tablet: New type of delivery system for hydrophobic drugs. Proc. Int. Symp Cont. Rel. Bioact. Mater. 28 (2001) 824-825
- B. Schwarz J. et al., Self-emulsifying controlled release tablet: New type of delivery system for hydrophobic drugs. Proc. Int. Symp Cont. Rel. Bioact. Mater. 27 (2000) 395-396
- C. WO0041676 A1
- D. WO9423700 A1
- E. FR2710535 A1
- F. Sugao H. et al., Taste masking of bitter drug powder without loss of bioavailability by heat treatment of waxcoated microparticles. J Pharm Sci., 87 (1998) 96-100

Documents A and B both refer to a self-emulsifying delivery system, where an active material is dissolved or dispersed in a lipid/surfactant phase to form a stable microemulsion. The microemulsion is granulated with gel forming water-soluble polymers and other excipients, dried, milled and compressed into traditional tablets.

The main difference between the present application documents A-B is the resulting type of delivery; according to the present application, a self emulsifying immediate release tablet is construed when a granulation medium containing lipophilic active substance, oil, surfactant and polar liquid is mixed with non-swellable filler and optionally binder, dried, milled and compressed into tablets. Documents A-B use the same method of manufacture, with a resulting controlledrelease tablet.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient. Continuation of: $Box\ V$

Document C discloses a self-emulsifying system for hydrophobic and water-sensitive agents. The system provides a solid dosage form, e.g. tablets. Microcrystalline cellulose is mixed with an oily substance, surfactant and water, granulated, extruded, spheronized and dried. The pellets so formed are suitable for tabletting or for filling into capsules. Thus, from document C, a process for the preparation of self-dispersing or self-emulsifying tablets is known.

The invention according to claims 1-5 moreover differs from documents A-C in that the surfactant is specified to be selected from the group consisting of fatty acid esters of glycerol, and fatty acid esters of polyethylene glycol. However, since these surfactants are well known to the person skilled in the art, this selection cannot in itself be considered to involve an inventive step.

Document D pertains to a solid preparation for substantially immediate release of an active agent with low or very low solubility. The composition according to document D does not include oil in the granulation medium. However, in other the process for production of preparation aspects, the corresponds to the method used according to the present application; i.e. solubilizing agents and water constitute the granulation medium, microcrystalline cellulose is a filler and pellet forming material. The granulation medium may be heated prior to addition to the filler. The active agent may form part of the granulation medium, or may be mixed with the filler prior to the addition of the granulation medium. Solubilizing agents include PEG 400 and PEG 40 hydrogenated castor oil.

In document E, a composition that is solid at room temperature, and liquid at body temperature, is produced from an active agent, a lipophilic phase, a surfactant and a cosurfactant. A microemulsion is formed when the composition is ingested. There is, however, no information as to how the composition is manufactured.

Document F concerns coating of a microparticle. The coating comprises hydrogenated oil and surfactants. The document is considered to disclose prior art and will not be further adressed.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient. Continuation of: $Box\ V$

Thus, all documents A-C pertain to processes for the preparation of self-dispersing or self-emulsifying tablets. These documents are considered to represent the closest prior art.

Documents A and B explicitly discloses a granulation medium in the form of a microemulsion. In document C, the type of lipophilic-hydrophilic dispersion is not identified. Thus, the difference between claims 3 and 4 of the present application, and the processes according to documents A-C is that claims 3-4 suggest that the granulation medium be an emulsion or a liquid crystal phase. However, the presence of all claims 2-4 implies that the type of lipophilic-hydrophilic dispersion is not central to the application, and therefore, these claims lack the requirement of inventive step.

In conclusion, claims 1-5 are new but lack the requirement of inventive step.



1. A process for the preparation of a self-dispersing or selfemulsifying immediate release tablet comprising the following steps,

mixing a granulation medium containing an active lipophilic substance with one or more non-swellable fillers and optional binders,

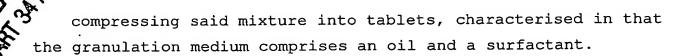
granulation of said mixture into granules,
drying of said granules,
sieving of the granules into a size below 1 mm,
mixing of the granules with tabletting aids, and
compressing said mixture into tablets, characterised in that
the granulation medium comprises an oil, a surfactant and a
polar liquid.

- 2. A process according to claim 1, characterised in that the granulation medium is a microemulsion.
- 3. A process according to claim 1, characterised in that the granulation medium is an emulsion.
- 4. A process according to claim 1, characterised in that the granulation medium is a liquid crystalline phase.
- 5. A process for the preparation of a self-dispersing immediate release tablet comprising the following steps,

mixing a heated granulation medium containing an active lipophilic substance with one or more non-swellable fillers and optional binders,

granulation of said mixture into granules which are allowed to cool,

sieving of the granules into a size below 1 mm, mixing of the granules with tabletting aids, and



- 6. A process according to any of claims 1-5, characterised in that the surfactant is selected from the group consisting of fatty acid esters of glycerol, and fatty acid esters of polyethylene glycol.
- 7. A tablet, characterised in being prepared by a process according to any of claims 1-6.

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